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Exercise Release of Cardiac Natriuretic Peptides Is Markedly Enhanced When Patients With Coronary Artery Disease Are Treated Medically by Beta-Blockers

We read with interest the recent study by Marie et al. (1), which concluded that patients with chronic coronary artery disease exhibited much higher exercise release of (ANP) and brain natriuretic peptide (BNP) when they were treated with beta-blockers. Exercise-related increase in natriuretic peptides had been reported across a majority of patients undergoing exercise treadmill test for evaluation of ischemic heart disease (2–5). The investigators postulated that the mechanisms of enhanced natriuretic peptide release secondary to beta-blockade may be related to exercise-induced increase in wall tension and cavity size. However, the researchers did not report the presence of reversible ischemia among the patients who were receiving beta-blocker therapy.

We recently reported (6) that exercise-induced increase in B-type natriuretic peptide was more prominent in patients with evidence of reversible ischemia on single-photon emission computed tomography (SPECT). It is therefore possible that the presence of exercise-induced reversible ischemia may serve as a confounding factor in this patient population, and we wonder whether the BNP rise among patients receiving beta-blockers during exercise is significant if the data are adjusted for presence of reversible ischemia.

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REPLY

When we started our study, we hoped that an enhanced secretion of atrial natriuretic peptide (ANP) and/or brain natriuretic peptide (BNP) might allow for detecting exercise ischemia. However, as it was already pointed out in our report, myocardial ischemia was documented by exercise-single-photon emission computed tomography (SPECT) in 63 of our 104 patients with coronary artery disease, and this ischemia was not a predictor of the exercise increase in blood levels of either ANP or BNP (1). More precisely, in the 63 patients with SPECT-ischemia, the difference between exercise and rest concentrations of BNP was, on average, 14 ± 20 ng/l. Equivalent values were observed in patients with normal SPECT: 14 ± 35 ng/l. By contrast, much higher values were observed in the remaining patients showing SPECT-necrosis: 49 ± 55 ng/l ($p < 0.001$).

As it was already discussed in our study (1), this is mainly an acute release of peptides from secretory granules that is likely to allow a prompt exercise rise in the blood concentrations of peptides. Therefore, this rise depends on 1) the amount of peptides, which may be previously stored within secretory granules, and 2) the mechanism of peptides release from these granules.

Granule storage is known to rise in parallel to the resting blood concentrations of natriuretic peptides and to the level of left ventricular dysfunction. This is presumably the reason why we found that the rest concentration of peptides was a main predictor of the exercise increase in peptide concentration. For both ANP and BNP, however, rest concentra-

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tions were related to age and to the extent of SPECT-necrosis, but not to exercise SPECT-ischemia.

As for the second point, exercise increases in heart rate and beta-blockers were the sole additional independent predictors of the exercise increase in peptide concentrations. Because both parameters were unrelated to the peptide concentrations at rest, we postulated that they might have a specific impact on the triggering of peptide release from secretory granules. For beta-blockers, this impact could be related not only to higher wall tension and cavity size at exercise, as mentioned in the letter by Drs. Win and Zoghbi, but mainly to an imbalance between alpha- and beta-adrenergic stimulations at exercise (1).

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